



PCT\_US\_10\_579104\_ST25.txt  
SEQUENCE LISTING

<110> POLYPHOR LTD.  
Universität Zürich  
<120> Template fixed beta-hairpin mimetics and their use in phage  
display

<130> P1338US

<140> PCT/US 10/579104  
<141> 2006-05-12

<150> PCT/EP 03/12783  
<151> 2003-11-15

<160> 44

<170> PatentIn version 3.5

<210> 1  
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<223> Key sequence known to occur in Platelet-Derived Growth Factor  
(PDGF), see Ross, R.; Raines, E. W.; Bowden-Pope, D.F.; Cell,  
1986, 46, 155-159.

<400> 1

Val Arg Lys Lys  
1

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<220>  
<223> Key sequence known to occur in Vasointestinal Peptide (VIP)  
showing neuroprotective properties against beta-amyloid  
neurotoxicity, see Proc. Natl. Am. Soc. USA, 1996, 96, 4143-4148.

<400> 2

Lys Lys Tyr Leu  
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<220>  
<223> Key sequence known to occur in integrin alpha.sub4 beta.sub1, see  
Europ. J. Biol., 1996, 242, 352-362 and Int. J. Pept. Prot. Res.,  
1996, 47, 427-436.

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Trp Leu Asp Val  
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<223> Key sequence known to occur in Factor Xa inhibitors, see Al  
Obeidis, F.; Ostrem, J. A.; Drug Discovery Today, 1998, 3,  
223-231.

<400> 4

Tyr Ile Arg Leu Pro  
1 5

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<213> Artificial Sequence  
  
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<223> Key sequence known to occur in laminine, see EMBO. J., 1984, 3,  
1463.

<400> 5

Tyr Ile Gly Ser Arg  
1 5

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<213> Artificial Sequence  
  
<220>  
<223> Key sequence known to occur in important physiologically active  
peptides, see Cell, 1987, 88, 989.

<400> 6

Ile Lys Val Ala Val  
1 5

<210> 7  
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<212> PRT  
<213> Artificial Sequence  
  
<220>  
<223> Key sequence known to occur in important physiologically active  
peptides, see J. Biol. Chem., 1998, 273, 11001-11006 and  
11007-11011.

<220>

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<221> misc\_feature  
<222> (4)..(5)  
<223> Xaa can be any naturally occurring amino acid

<400> 7

Pro Pro Arg Xaa Xaa Trp  
1 5

<210> 8  
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<212> PRT  
<213> Artificial Sequence

<220>  
<223> Hairpin mimetic derived from the general formula Cys-Z-Cys  
wherein the alpha amino group of the first amino acid is  
acetylated and wherein Z consists of 8 amino acids.

<220>  
<221> DISULFID  
<222> (1)..(10)

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
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<400> 8

Cys Lys Trp Phe Leu Ala His Tyr Ala Cys  
1 5 10

<210> 9  
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<212> PRT  
<213> Artificial Sequence

<220>  
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2  
wherein the alpha amino group of the first amino acid is  
acetylated, wherein Z consists of 8 amino acids, and wherein both  
R1 and R2 consist of 2 amino acids.

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> DISULFID  
<222> (3)..(12)

<400> 9

Glu Thr Cys Lys Trp Phe Leu Ala His Tyr Ala Cys Thr Lys  
1 5 10

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<210> 10  
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<213> Artificial Sequence

<220>  
<223> hairpin mimetic derived from the general formula Cys-Z-Cys  
wherein the alpha amino group of the first amino acid is  
acetylated and wherein Z consists of 10 amino acids.

<220>  
<221> DISULFID  
<222> (1)..(12)

<220>  
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<222> (1)..(1)  
<223> ACETYLATION

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Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys  
1 5 10

<210> 11  
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<220>  
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2  
wherein the alpha amino group of the first amino acid is  
acetylated, wherein Z consists of 10 amino acids, and wherein  
both R1 and R2 consist of 2 amino acids.

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> DISULFID  
<222> (3)..(14)

<400> 11

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1 5 10 15

<210> 12  
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<212> PRT  
<213> Artificial Sequence

<220>  
<223> Hairpin mimetic derived from the general formula Cys-Z-Cys  
wherein the alpha amino group of the first amino acid is  
acetylated and wherein Z consists of 10 amino acids.

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<220>  
<221> DISULFID  
<222> (1)..(12)

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<222> (1)..(1)  
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<210> 13  
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<220>  
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2  
wherein the alpha amino group of the first amino acid is  
acetylated, wherein Z consists of 10 amino acids, and wherein  
both R1 and R2 consist of 2 amino acids.

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> DISULFID  
<222> (3)..(14)

<400> 13

Leu Glu Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Lys Val  
1 5 10 15

<210> 14  
<211> 16  
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<220>  
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2  
wherein the alpha amino group of the first amino acid is  
acetylated, wherein Z consists of 10 amino acids, and wherein  
both R1 and R2 consist of 2 amino acids.

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> DISULFID  
<222> (3)..(14)

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<400> 14

Asn Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Lys Val  
1 5 10 15

<210> 15

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2  
wherein the alpha amino group of the first amino acid is  
acetylated, wherein Z consists of 10 amino acids, and wherein  
both R1 and R2 consist of 2 amino acids.

<220>

<221> MOD\_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> DISULFID

<222> (3)..(14)

<400> 15

Gly Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly Gly  
1 5 10 15

<210> 16

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2  
wherein the alpha amino group of the first amino acid is  
acetylated, wherein Z consists of 10 amino acids, and wherein  
both R1 and R2 consist of 2 amino acids.

<220>

<221> MOD\_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> DISULFID

<222> (3)..(14)

<400> 16

Glu Thr Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Thr Lys  
1 5 10 15

<210> 17

<211> 18

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<212> PRT  
<213> Artificial Sequence

<220>  
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> DISULFID  
<222> (4)..(15)

<400> 17

Glu Leu Lys Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys Glu  
1 5 10 15

Val Lys

<210> 18  
<211> 18  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> DISULFID  
<222> (4)..(15)

<400> 18

Lys Val Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly  
1 5 10 15

Leu Glu

<210> 19  
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<212> PRT

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<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>

<221> MOD\_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> DISULFID

<222> (4)..(15)

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Gly Gly Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly  
1 5 10 15

Gly Gly

<210> 20

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 12 amino acids.

<220>

<221> DISULFID

<222> (1)..(14)

<220>

<221> MOD\_RES

<222> (1)..(1)

<223> ACETYLATION

<400> 20

Cys Gly Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Gly Cys  
1 5 10

<210> 21

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 12 amino acids, and wherein

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both R1 and R2 consist of 2 amino acids.

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> ACETYLATION

<220>  
<221> DISULFID  
<222> (3)..(16)

<400> 21

Glu Thr Cys Gly Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Gly Cys  
1 5 10 15

Thr Lys

<210> 22  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Core peptide sequence Z taken from the CDR L3 loop of an antibody  
described in Jiang, L. et al., Chimia, 2000, 54, 558-563.

<400> 22

Leu Trp Tyr Ser Asn His Trp Val  
1 5

<210> 23  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Modified core peptide sequence Z derived from core peptide  
sequence with the SEQ ID NO:22 containing a stabilizing beta-turn  
and a beta-sheet sequence according to Chou, P. Y., Fasman, G.  
D., J. Mol. Biol., 1977, 115, 135-175.

<400> 23

Lys Trp Phe Ser Asn His Tyr Gln  
1 5

<210> 24  
<211> 6  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Core peptide sequence Z constructed from peptide with the SEQ ID  
NO:25.

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<400> 24

Phe Leu Ala His Tyr Ala  
1 5

<210> 25

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Oligopeptide which does not contain a dedicated stabilizing beta-turn sequence or a beta-sheet sequence according to Chou, P. Y., Fasman, G. D., J. Mol. Biol., 1977, 115, 135-175.

<400> 25

Leu Trp Tyr Ser Asn His Trp Val Lys Trp  
1 5 10

<210> 26

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide No. 1 used to construct insert DNA coding for template fixed hairpin mimetic of SEQ ID NO:10 and used to construct insert DNA coding for randomized library template fixed beta-hairpin mimetics having sequences according to SEQ ID NO:42.

<400> 26

catgccccggg tacctttcta ttctcactct gaaacacctgc 39

<210> 27

<211> 84

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide No. 2 used to construct insert DNA coding for template fixed hairpin mimetic of SEQ ID NO:10.

<400> 27

catgttccgg ccgagccacc acctttggtg caggtctgat aatggttgct gaaccatttg 60

gtgcagggtt cagagtgaga atag

84

<210> 28

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> DNA sequence coding for the peptide shown in SEQ ID NO:8.

<400> 28

tgcaaatggt tcctggcgca ttatgcgtgc 30

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<210> 29  
<211> 42  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:9.

<400> 29  
gaaaacctgca aatggttcct ggcgcattat gcgtgcacca aa 42

<210> 30  
<211> 36  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:10.

<400> 30  
tgcaccaaat gtttcagcaa ccattatcg acctgc 36

<210> 31  
<211> 48  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:11.

<400> 31  
gaaacctgca ccaaattgggtt cagcaaccat tatcagacct gcaccaaa 48

<210> 32  
<211> 36  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:12.

<400> 32  
tgcaccaaat gtttcctggc gcattatcg acctgc 36

<210> 33  
<211> 48  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:13.

<400> 33  
ctggaatgca ccaaattgggtt cctggcgcat tatgcgacct gcaaagtt 48

<210> 34  
<211> 48

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<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:14.

<400> 34  
aacgggttgca ccaaatggtt cctggcgcat tatgcgacct gcaaagtt 48

<210> 35  
<211> 48  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:15.

<400> 35  
ggtgggttgca ccaaatggtt cctggcgcat tatgcgacct gcggcggt 48

<210> 36  
<211> 48  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:16.

<400> 36  
gaaaccttgca ccaaatggtt cctggcgcat tatgcgacct gcacccaaa 48

<210> 37  
<211> 54  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:17.

<400> 37  
gaactgaaat gcacccaaatg gttcagcaac cattatcaga cctgcgaagt taaa 54

<210> 38  
<211> 54  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:18.

<400> 38  
aaagttgggtt gcacccaaatg gttcctggcg cattatgcga cctgcggtct ggaa 54

<210> 39  
<211> 54  
<212> DNA  
<213> Artificial Sequence

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<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:19.

<400> 39  
ggtgttggct gcaccaaatg gttcctggcg cattatgcga cctgcggcgg tggt 54

<210> 40  
<211> 42  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:20.

<400> 40  
tgcgttacca aatggttcag caaccattat cagaccgtt gc 42

<210> 41  
<211> 54  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence coding for the peptide shown in SEQ ID NO:21.

<400> 41  
gaaacctgcg gtaccaaatg gttcagcaac cattatcaga ccggttgcac caaa 54

<210> 42  
<211> 48  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> DNA sequence of randomized template fixed beta-hairpin mimetic Phage library.

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<223> n is a, c, g, or t

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<222> (13)..(14)  
<223> n is a, c, g, or t

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<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (28)..(29)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature

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<222> (31)..(32)  
<223> n is a, c, g, or t

<220>  
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<222> (34)..(35)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (37)..(38)  
<223> n is a, c, g, or t

<400> 42  
gaaacctgcn nknnknnkcg tggtgacnnk nnknnknnkt gcaccaaa

48

<210> 43  
<211> 16  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Translated protein sequence of a randomized template fixed  
beta-hairpin mimetic phage library

<220>  
<221> DISULFID  
<222> (3)..(14)

<220>  
<221> MISC\_FEATURE  
<222> (4)..(6)  
<223> Xaa can be any naturally occurring amino acid

<220>  
<221> MISC\_FEATURE  
<222> (10)..(13)  
<223> Xaa can be any naturally occurring amino acid

<400> 43

Glu Thr Cys Xaa Xaa Xaa Arg Gly Asp Xaa Xaa Xaa Xaa Cys Thr Lys  
1 5 10 15

<210> 44  
<211> 84  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Oligonucleotide No. 3 used to construct insert DNA coding for  
randomized library template fixed beta-hairpin mimetics having  
sequences according to SEQ ID NO:42.

<220>  
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<220>  
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<220>  
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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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nngcaggttt cagagtgaga atag 84